Non-technical Abstract

Malignant gliomas are the most common brain tumors in adults with 10,000 to 15,000 new cases every year (Levine et al.,1989). Treatments such as surgery, radiation, and chemotherapy, have extended the survival of patients with these brain tumors from 14 weeks to one year; however, the five year survival rate for one type of malignant glioma, glioblastoma multiforme, is still 5.5% or less. The disease is characterized by local tumor recurrence with relentless regrowth, increasing symptoms, and ultimately death. Thus, new treatments for malignant gliomas are needed.

The proposed clinical trial, NG1-003, will study the safety and effectiveness of an engineered herpes virus, G207, administered directly into the brain of subjects with brain tumors. G207, the virus to be used in this study, has been modified from the herpes virus that causes cold sores (called herpes simplex virus type 1 or HSV-1). G207 has been designed so that it will kill tumor ceils, but not normal brain cells. The safety of G207 has been shown in animals and in previous studies in humans with brain tumors.

In previous phase 1 clinical trials, a total of 22 subjects with brain tumors that recurred after initial treatment received G207, which was injected directly into their tumor. G207 was generally well tolerated and safe. To date, 19 of these subjects have died of their disease, one subject died from a side effect of radiation therapy, and two subjects remain alive.

MediGene, Inc. would like to continue to study G207 as therapy in subjects who have brain tumors that have recurred after initial treatment. Protocol NG1-003 is a phase lb/II study, wherein up to 21 subjects will be enrolled in the phase lb portion and will receive doses of G207 that are higher than tested in the previous trials. The objectives of NG1-003 (phase 1b are to determine the safety and tolerability of G207, and to ascertain whether or not G207 replicates within tumor tissue. Another objective is to define the dose to be used in the phase II portion of NG1-003.

Subjects in the phase I portion of NG1-003 will receive G207 in **a** fractionated manner. Initially, 15% of the total dose will be injected into the tumor. Two days later the tumor will be removed and the remaining G207 dose will be injected into the brain area surrounding the site of the tumor. Subjects will be monitored and clinical assessments will be performed at specific study timepoints.

After three months of evaluation, subjects will be followed for safety and survival in a long-term protocol, NG1-004. for up to 12 months and, thereafter, by telephone. Results from the phase lb portion of NGI-003 will be reviewed. The phase II portion of NG1-003 will only commence provided that there are no safety or other concerns.

The design of the phase II portion of protocol NG1-003 is a classic NIH, two-stage study and will be conducted at several clinical study sites. The objectives are to assess the safety of G207 and subject survival at six months. Enrollment of up to 14 subjects is

planned for stage one. Additional subjects will be enrolled (up to 30 subjects and 44 overall) in stage II if there is a survival benefit for up to five subjects for six months or longer in stage one. Participants will receive a single dose of G207 at the dose determined from phase lb. The tumor will be removed, and G207 will be injected into the brain area surrounding the tumor. Again, subjects will be monitored and clinical assessments will be performed at specific study timepoints. After six months of evaluation, subjects will be followed for safety and survival in a long-term protocol, NG1-005, for up to 12 months and, thereafter, by telephone.

Literature Cited

Levine et al. Cancer: *Prin. & Prac. Of Onc*., 1557-1611 (1989)